

SUBSTITUTED 4(5H)-OXAZOLONES AND THEIR SALTS.

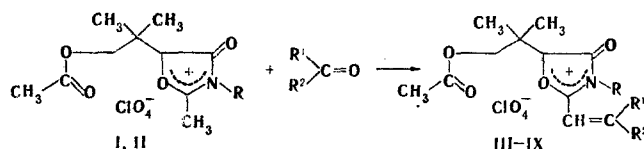
2.* SYNTHESIS OF 2-[β-ALKYL(ARYL OR FURYL)VINYL]-5-(1,1-DIMETHYL-2-ACETOXYETHYL)-4(5H)-OXAZOLONIUM PERCHLORATES

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UDC 547.787.07

2,3,5-Substituted 4(5H)-oxazolonium perchlorates were obtained by condensation of 2-methyl-substituted 4(5H)-oxazolonium perchlorates with aromatic and furan aldehydes and ketones and acetone, and their IR, UV, and PMR spectral characteristics were investigated.

4(5H)-Oxazolonium salts constitute a class of organic compounds to which little study has been devoted [2-4]. A number of new 2-[β-alkyl(aryl or furyl)vinyll]-4(5H)-oxazolonium perchlorates (IIIa-e, IV, Va-g, VI, VIIa-f, VIII, and IX; Table 1) were synthesized during a study of the reactivities of 2-methyl-substituted 4(5H)-oxazolonium salts I and II, which we previously obtained in [2]. This reaction is classified as an example of the well-known



I R=H; II R=CH₃; III, IV R=H; III R¹=H, a R²=C₆H₅; b R²=CH=CHC₆H₅; c R²=4-OCH₃C₆H₄; d R²=4-BrC₆H₄; e R²=3-NO₂C₆H₄; IV R¹=H, R²=5-methyl-2-furyl; V-IX R=CH₃; V R¹=H, a R²=C₆H₅; b R²=CH=CHC₆H₅; c R²=4-OCH₃C₆H₄; d R²=4-BrC₆H₄; e R²=3-NO₂C₆H₄; f R²=4-NO₂C₆H₄; g R²=2-NO₂C₆H₄; VI R¹=CH₃, R²=C₆H₅; VII R¹=H, a R²=2-furyl; b R²=vinyl-2-furyl; c R²=5-methyl-2-furyl; d R²=5-bromo-2-furyl; e R²=5-iodo-2-furyl; f R²=5-nitro-2-furyl; VIII R¹=CH₃, R²=5-methyl-2-furyl; IX R¹=CH₃, R²=CH₃

acid-catalyzed aldol-crotonic condensation [5-7].

The conditions under which the synthesis of salts III-IX are carried out, the reaction rates, and the yields of substances depend substantially on the structures of the starting compounds. The condensation of perchlorates I and II proceeds most smoothly with aromatic aldehydes. Compounds IIIa-d and Va-d are readily formed by heating solutions of starting salts I and II with the corresponding aldehydes in a mixture of glacial acetic acid and acetic anhydride (2:1) to the boiling point; higher yields are obtained with perchlorate II. All of the substituents in the benzene ring of the aldehyde that have a +M effect (RO- and Hal-) promote the reactions, whereas a nitro group (-I and -M effects) lower the reactivity of the aldehyde so much that the reaction does not take place under the indicated conditions. Compounds IIIe and Ve-g can be obtained by refluxing the reaction mixture for 30 min. All three nitrobenzaldehydes react with the more active N-substituted perchlorate II to give condensation products; however, the yields of ortho and para isomers Vf, g are substantially lower than the yield of Ve based on m-nitrobenzaldehyde. All of the information given above indicates the decisive influence of the M effect on the course of the reaction.

In contrast to I and its close analogs, viz., 2-alkyl-4-oxo-1,3-benzoxazinonium salts [8], perchlorate II undergoes reaction with ketones, and this indicates its high reactivity with oxo compounds. Salts VI and IX were obtained in the presence of catalytic amounts of HCl by refluxing the reaction mixture for 90 min.

*See [1] for Communication 1.

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TABLE 1. Characteristics of 2,3,5-Substituted 4(5H)-Oxazoloniium Perchlorates

Com- pound	O p H	Crystal color	IR spectrum, ν , cm^{-1}			UV spectrum, λ_{max} (log ϵ), nm		Found. %			Empirical formula ^a	Calc., %			Yield, %		
			amide C=O	O—C—N	C=C	ester C=O	in acetic acid	in acetic acid + HClO ₄ (10 mmole/liter)	C	H		Cl	N	C		H	Cl
IIIa	135	Light Yellow	1810	1580, 1525	1610	1735	318 (4,40)	352 (4,42)	50,6	4,8	8,6	3,3	50,8	5,0	8,8	3,5	66
IIIb	180	Yellow	1790	1580, 1540	1600	1730	354 (4,59)	406 (4,50) ^d	53,6	5,0	8,5	3,5	53,3	5,2	8,3	3,3	72
IIIc	184	"	1800	1600, 1560	1630	1740	356 (4,56)	413 (4,56)	49,7	5,1	8,5	3,4	50,1	5,1	8,2	3,2	92
IIId	190	"	1770	1560, 1550	1625	1720	326 (4,52)	362 (4,57)	42,4	4,2	24,1	3,1	42,5	4,0	24,0	2,9	81
IIIe	142	White	1815	1560, 1530	1635	1730	300 (4,41)	327 (4,42)	45,3	4,7	7,8	5,9	45,7	4,3	7,9	6,3	10
IV	154 ^c	Green	1800	1590, 1550	1620	1730	372 (4,64)	425 (4,83)	47,8	4,8	8,5	3,5	47,4	5,0	8,7	3,4	40
Va	162	Yellow	1800	1570, 1550	1630	1730	358 (4,09)	358 (4,37)	51,8	5,7	8,8	3,6	52,0	5,3	8,5	3,4	80
Vb	185	Red	1800	1580, 1530	1600	1730	412 (4,49)	412 (4,56)	54,2	5,8	8,0	3,2	54,4	5,5	8,0	3,2	72
Vc	188	Yellow	1780	1580, 1540	1620	1720	420 (4,23)	420 (4,16) ^d	50,9	5,4	7,7	3,5	51,2	5,4	7,9	3,1	98
Vd	211	Yellow	1800	1570, 1540	1630	1730	370 (3,68)	370 (4,15)	43,9	4,2	22,9	3,0	43,7	4,3	23,3	2,8	92
Ve	180	White	1800	1570, 1530	1630	1720	335 (3,72)	335 (4,17)	46,8	4,8	8,0	5,8	46,9	4,6	7,7	6,1	65
Vf	188	"	1820	1570, 1530	1640	1730	295 (3,79)	—	46,7	4,6	7,5	5,7	46,9	4,6	7,7	6,1	42
Vg	150	"	1800	1590, 1520	1630	1760	—	—	46,4	4,5	7,7	5,8	46,9	4,6	7,7	6,1	30
VI	123	Yellow	1770	1595, 1530	1630	1730	364 (3,90); 337 (3,85)	—	53,0	5,3	8,4	3,6	53,1	5,6	8,2	3,3	37
VIIa	100 ^c	Green	1770	1580, 1550	1620	1750	400 (3,94)	—	47,0	4,9	8,5	3,4	47,4	5,0	8,7	3,4	40
VIIb	110 ^c	Red	1770	1590, 1550	1620	1730	460 (4,27)	—	50,1	5,2	8,0	3,2	50,0	5,1	8,2	3,2	70
VIIc	171	Green	1800	1590, 1560	1630	1760	431 (4,57)	431 (4,82) ^d	48,4	5,2	8,2	3,5	48,6	5,3	8,4	3,3	68
VIIId	173	"	1800	1595, 1520	1620	1760	418 (4,05)	—	39,9	4,3	23,7	3,0	39,7	4,0	23,8	2,9	62
VIIe	178	Yellow	1790	1580, 1550	1620	1750	430 (4,18)	—	35,9	3,8	30,1	2,6	36,1	3,6	30,5	2,6	68
VIIIf	106	White	1780	1595, 1540	1630	1740	350 (3,52)	—	43,0	4,3	8,0	6,2	42,6	4,2	7,9	6,2	15
VIIIf	118	Green	1780	1590, 1540	1610	1740	436 (3,81); 332 (3,42)	—	50,0	5,6	8,0	3,2	49,8	5,6	8,2	3,2	27
IX	150	White	1770	1550, 1530	1660	1730	285 (4,15)	—	45,6	5,9	9,5	3,8	45,7	6,0	9,6	3,8	44

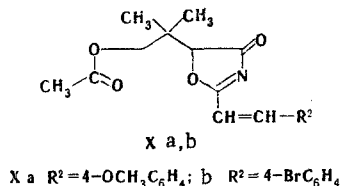
^aIn the case of compounds that contain Br or I the empirical formulas were calculated on the basis of Cl + Br or Cl + I, respectively. ^bThese compounds were purified by recrystallization from glacial acetic acid. ^cThese compounds were purified by recrystallization from chloroform-ether. ^dThese UV spectra were obtained from solutions in acetic acid containing 1 mmole/liter HClO₄.

For the first time for carbonium ions we carried out the condensation of salts I and II with oxo compounds of the furan series and obtained the previously undescribed 2-(β -furyl-vinyl)-4(5H)-oxazolonium perchlorates IV, VIIa-f, and VIII. In contrast to oxo compounds of benzene, the reaction is complicated by simultaneous resinification, which lowers the yields of furyl-substituted salts VIIa, b, d, f as compared with the yields of the corresponding salts Va, b, d, f of the benzene series. The above-indicated method for the reaction with aromatic aldehydes was found to be applicable only in reactions of 5-substituted furfurals with perchlorate II, i.e., in the synthesis of VIIc-f. Instantaneous resinification occurs in the preparation of salts IV and VIIa, b; we were able to avoid this by carrying out the reaction under milder conditions (at 40-50°C in glacial acetic acid or 1,4-dioxane for 10 min). Acetic anhydride evidently leads to acylation of the furfurals [9], and this accelerates the resinification process. In the case of the reaction of perchlorate I with furfural and furylacrolein in glacial acetic acid we were unable to isolate the corresponding vinyl-substituted salts at all, despite the fact that characteristic maxima in the UV spectra of the reaction mixture provided evidence for their formation.

The IR spectra of salts III-IX (Table 1) contain two clearly distinguishable bands of two different oxo groups, viz., the amide group of the heteroring and the ester group of the side chain. The high frequency of absorption of the carbonyl group of the heteroring (1770-

1820 cm^{-1}) is due to interaction with the electron-acceptor $\text{O}=\text{C}=\text{N}^+$ fragment of the molecule; this also explains the dependence of this band on the character of the electronic effects of the substituents in the side chain attached to C_2 . The amide band in the spectra of 2-vinyl-substituted salts III-IX is shifted an average of 10-50 cm^{-1} as compared with the $\nu_{\text{C}=\text{O}}$ band (1830 cm^{-1}) of starting perchlorates I and II [2]. The frequency of the vibrations of the ester carbonyl group also varies as a function of the substituent attached to the C_2 atom of the heteroring over a rather wide range (1720-1760 cm^{-1}). This may constitute evidence for the existence of an intermolecular or intramolecular donor-acceptor interaction between the ester $\text{C}=\text{O}$ group and the carbonium fragment of the heteroring. The $\text{O}=\text{C}=\text{N}^+$ fragment shows up in the spectra of salts III-IX as two bands of skeletal vibrations at 1525-1590 cm^{-1} . The $\text{C}=\text{C}$ bond attached to the C_2 atom of the heteroring, which is conjugated with the aromatic ring, shows up in the form of one intense band at 1600-1640 cm^{-1} , whereas in the case of 2-(β, β' -dimethylvinyl)-substituted salt IX, in which no such conjugation is present, it shows up at 1660 cm^{-1} . Considerable absorption of the stretching vibrations of the ClO_4^- anion is observed at 1100 cm^{-1} in the spectra of the salts.

We investigated the UV spectra of perchlorates III-IX in glacial acetic acid (Table 1). The UV spectra in glacial CH_3COOH of salts III-V, VII, and IX, obtained by condensation of salts I and II with aldehydes or acetone, contain only one absorption band, which corresponds to a $\pi \rightarrow \pi^*$ electron transition of the entire conjugated system of the 2-substituted 4(5H)-oxazolonium salt (K band). Another K band is present in the spectra of salts VI and VIII obtained by condensation of perchlorate II with ketones. These substances are evidently a mixture of isomers, for example, geometrical isomers (cis and trans). The UV spectra of NH perchlorates IIIa-e and IV (Table 1) in glacial acetic acid differ substantially from the UV spectra of NCH_3 perchlorates Va-e and VIIc, which are similar to them with respect to their electronic structures. To clear up this anomaly we recorded the UV spectra of our previously synthesized 4(5H)-oxazolones Xa, b in glacial acetic acid [10]:



It was found that the UV spectra of these compounds [Xa, λ_{max} 356 nm ($\log \epsilon$ 4.60); Xb, λ_{max} 326 nm ($\log \epsilon$ 4.58)] coincide with the spectra of the analogous perchlorates IIIc, d, except for a certain deviation in the extinctions. The latter indicates that NH 4(5H)-oxazolonium salts III and IV are converted primarily to the corresponding 4(5H)-oxazolones (A) when they are dissolved in a polar solvent:

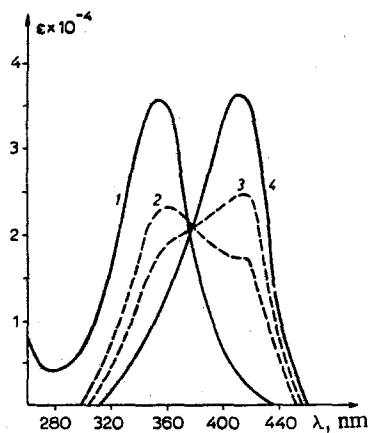


Fig. 1

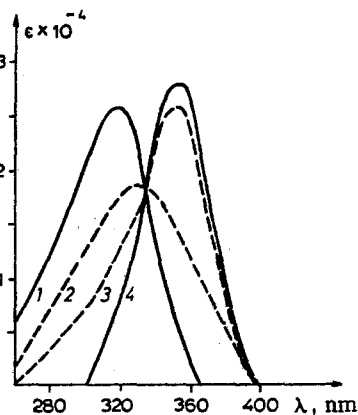
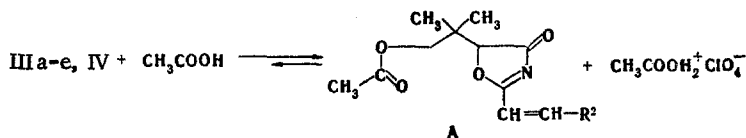


Fig. 2

Fig. 1. UV spectra of salt IIIc in glacial acetic acid containing various amounts of HClO_4 ($\text{CHClO}_4 \cdot 10^4$ moles/liter): 1) 0.0; 2) 5.0; 3) 5.5; 4) 10.0.

Fig. 2. UV spectra of salt IIIa in glacial acetic acid containing various amounts of HClO_4 ($\text{CHClO}_4 \cdot 10^4$ moles/liter): 1) 0.0; 2) 10.0; 3) 100.0; 4) 1000.0.



In fact, whereas the position of the K band of NCH_3 salts Va-e and VIIc does not depend on the presence of perchloric acid in solution, the UV spectra of NH perchlorates IIIa-e and IV change substantially. For example, a new long-wave K band appears in the spectra of perchlorate IIIc (Fig. 1) as the perchloric acid concentration increases. The isobestic point provides evidence that the salt is converted quantitatively to an oxazolone. The UV spectra of salts IIIb and IV change similarly. A somewhat different character of the change in the UV spectra under the influence of HClO_4 is observed in the case of salts IIIa, d, e (Fig. 2). In the spectra of these compounds one observes a gradual bathochromic shift of the K band; this is evidently associated with the closely located initial and newly developing K bands (Table 1). The regularities indicated above express a shift of the equilibrium to the left under the influence of perchloric acid in accordance with the Le Chatelier-Brown principle. When hydrochloric or sulfuric acid is used in place of perchloric acid, the character of the UV spectra of NH salts IIIa-e and IV changes similarly. In chloroform or 1,4-dioxane NH salts III and IV are also converted to 4(5H)-oxazolones (A). Thus the UV spectrum of salt IIIc has λ_{max} ($\log \epsilon$) 348 (4.34) and 345 nm (4.64).

It becomes clear why furfurals were particularly acidophobic in reactions with salt I. The perchloric acid present in the reaction mixture promotes resinification, particularly when acetic anhydride is present [9]. The K band of perchlorates III-IX is shifted to the long-wave region of the spectrum as the donor properties of substituent R^2 increase. This regularity is also confirmed by a comparison of the position of the bands of the corresponding phenyl- and furyl-substituted perchlorates Va, b and VIIa, b (Table 1), since the furan ring is capable of shifting the electrons more readily than the benzene ring [11].

In the PMR spectrum (in CF_3COOH , Fig. 3) of perchlorates IIIc, d the 5-H proton attached to the chiral carbon atom gives a singlet at 5.22 ppm; this constitutes evidence for the presence of a positive charge in the ring, since it is shifted substantially to strong field ($\Delta\delta$ 1.23 ppm) in the spectrum of corresponding oxazolone Xa [10]. The chirality of the C_5 atom leads to anisochronicity of the gem-dimethyl grouping in the side chain. The methylene protons in the β position relative to C_5 are diastereotopic and resonate in the form of an AB quartet with geminal constant $^2J_{\text{HH}} = 11.9$ Hz. Vicinal spin-spin coupling constant $^3J_{\text{AB}} = 15.6$ Hz of the olefin protons attests to their trans configuration.

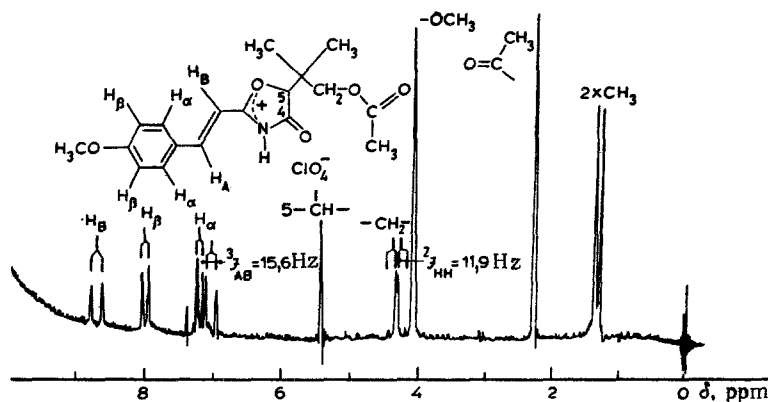


Fig. 3. PMR spectrum of salt IIIc.

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with Specord and UR-20 spectrometers. The UV spectra were recorded with Specord and VSU2-P spectrophotometers. The PMR spectra of solutions in trifluoroacetic acid were recorded with a Varian HA-100D spectrometer.

Perchlorate I was obtained by the method in [2], and the 4(5H)-oxazolones were obtained by the method in [10]. The solutions of HClO_4 in acetic acid were prepared by the method in [12].

2-[\beta-(4-Bromophenyl)vinyl]-5-(1,1-dimethyl-2-acetoxyethyl)-4(5H)-oxazolonium Perchlorate (IIIc). A mixture of 3.13 g (0.01 mole) of perchlorate I, 2.04 g (0.011 mole) of p-bromobenzaldehyde, 2 ml of acetic anhydride, and 4 ml of glacial acetic acid was heated to the boiling point, after which it was cooled and diluted with ether. The precipitated crystals were removed by filtration and washed with ethyl acetate and ether. The yield was 4 g. Compounds IIIa-c, Va-d, and VIIc-e (Table 1) were similarly obtained.

2-(\beta,\beta'-Dimethylvinyl)-5-(1,1-dimethyl-2-acetoxyethyl)-3-methyl-4(5H)-oxazolonium Perchlorate (IX). A mixture of 3.23 g (0.01 mole) of perchlorate II, 1 g (0.017 mole) of acetone, 2 ml of acetic anhydride, 4 ml of glacial acetic acid, and two drops of concentrated HCl was refluxed for 90 min. It was then cooled and treated with ethyl acetate, and the mixture was allowed to stand in a refrigerator for 15 min. The precipitated crystals coagulated after the addition of ether. They were removed by filtration and washed with ethyl acetate and ether. The yield was 1.6 g. Compound VI was similarly obtained. Data on VI and IX are presented in Table 1.

2-[\beta-(5-Methyl-2-furyl)vinyl]-5-(1,1-dimethyl-2-acetoxyethyl)-4(5H)-oxazolonium Perchlorate (IV). A 3.13-g (0.01 mole) sample of perchlorate I was dissolved by heating in 8 ml of 1,4-dioxane or 5 ml of glacial acetic acid, 1.1 ml (0.011 mole) of 5-methylfurfural was added dropwise at 40-50°C, and the mixture was maintained at this temperature for 30 min. It was then cooled and treated with ether, and the solvent was removed from the precipitated dark oil by decantation. The oil was crystallized in the cold in 20 ml of ethyl acetate. The substance was removed by filtration and washed with ethyl acetate and ether. The yield was 1.6 g. Compounds VIIa, b were similarly obtained. Perchlorate VIII was similarly synthesized by heating the reaction components for 1 h. Data on VIIa, b, IV, and VIII are presented in Table 1.

2-[\beta-(3-Nitrophenyl)vinyl]-3-methyl-5-(1,1-dimethyl-2-acetoxyethyl)-4(5H)-oxazolonium Perchlorate (Ve). A mixture of 3.23 g (0.01 mole) of salt II, 1.66 g (0.011 mole) of 3-nitrobenzaldehyde, 2 ml of acetic anhydride, and 4 ml of glacial acetic acid was refluxed for 30 min, after which it was cooled and treated with ethyl acetate and ether. The precipitated crystals were removed by filtration and washed with ether. The yield was 3 g. Compounds IIIe, Vf, g, and VIIf (Table 1) were similarly obtained.

2,3-Dimethyl-5-(1,1-dimethyl-2-acetoxyethyl)-4(5H)-oxazolonium Perchlorate (II). This compound was obtained by our modified method [2]. A 3-ml (0.03 mole) sample of 70% HClO_4 was added dropwise with cooling to 0°C to a mixture of 4.83 g (0.03 mole) of β,β -dimethyl- α,γ -dihydroxybutyric acid N-methylamide and 18 ml of acetic anhydride, after which the mixture was heated to the boiling point and refluxed for 3 min. It was then cooled to room

temperature and diluted with ether. The precipitated crystals were washed successively with glacial acetic acid and ether to give 5.2 g (53%) of snow-white crystals of II with mp 165°C (from glacial acetic acid). IR spectrum: 1830 (C=O); 1740 (O-C=O); 1610, 1530 (O=C=N⁺); 1100 cm⁻¹ (ClO₄⁻). Found: C 40.6; H 5.7; Cl 11.0; N 4.3%. C₁₁H₁₈ClNO₈. Calculated: C 40.3; H 5.5; Cl 10.8; N 4.3%.

LITERATURE CITED

1. T. P. Kosulina, Z. I. Zelikman, and V. G. Kul'nevich, Zh. Org. Khim., 12, 1134 (1976).
2. T. P. Kosulina, Z. I. Zelikman, and V. G. Kul'nevich, USSR Inventor's Certificate No. 537598 (1975); Byull. Izobr., No. 3, 235 (1979).
3. G. N. Dorofeenko, V. D. Karpenko, and Yu. I. Ryabukhin, Khim. Geterotsikl. Soedin., No. 5, 702 (1977).
4. G. N. Dorofeenko, V. D. Karpenko, and Yu. I. Ryabukhin, Zh. Org. Khim., 14, 1904 (1978).
5. H. Becker, Introduction to the Electronic Theory of Organic Reactions [Russian translation], Mir, Moscow (1977), p. 317.
6. G. N. Dorofeenko, L. V. Mezheritskaya, and Yu. I. Ryabukhin, Zh. Org. Khim., 9, 390 (1973).
7. Yu. I. Ryabukhin, V. V. Mezheritskii, V. D. Karpenko, and G. N. Dorofeenko, Khim. Geterotsikl. Soedin., No. 9, 1184 (1975).
8. V. V. Mezheritskii, L. G. Minyaeva, Yu. I. Ryabukhin, and G. N. Dorofeenko, Khim. Geterotsikl. Soedin., No. 3, 328 (1977).
9. G. N. Dorofeenko and V. I. Karaban, Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol., 7, 432 (1964).
10. T. P. Kosulina, Dissertation Abstracts (Master's Degree) [in Russian], Rostov-on-Don (1977), p. 17.
11. R. A. Gavar, V. A. Zilitis, Ya. P. Stradyn', and S. A. Giller, Khim. Geterotsikl. Soedin., No. 1, 3 (1971).
12. I. Gyenes, Titration in Nonaqueous Media, Krieger (1968).

RESEARCH ON AMINOMETHYLENE DERIVATIVES OF AZOLES.

24.* CYCLIZATION OF THIOHIPPURIC ACID IN THE PRESENCE OF THE VILSMEIER REAGENT

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and A. V. El'tsov

UDC 547.787.2'789.5

It is shown that, in contrast to hippuric acid, thiohippuric acid reacts with dimethylformamide in the presence of phosphorus oxychloride to give three compounds, viz., 2-phenyl-4-dimethylaminomethylene-5-thiazolone, 2-phenyl-4-dimethylaminomethyleneoxazole-5-thione, and 2-phenyl-4-formyl-5-chlorothiazole. The pathways of their formation are discussed. The structures of the compounds obtained and some transformations of 2-phenyl-4-formyl-5-chlorothiazole were studied. 2-Phenyl-4-formyl-5-hydroxy(mercapto)thiazoles and their methyl derivatives, as well as 2-phenyl-4-dimethylaminomethylenethiazole-5-thione, were synthesized from the latter.

Hippuric acid readily undergoes cyclodehydration in the presence of N-methylformanilide and phosphorus oxychloride to 2-phenyl-5-oxazolone, which is then aminoformylated to give an aminomethylene derivative (I) [2]. The reaction of hippuric acid with the adduct from dimethylformamide (DMF) and phosphorus oxychloride proceeds similarly and leads to II.

We used thiohippuric acid to obtain 2-phenyl-4-dimethylaminomethylene-5-thiazolone (III) under the conditions of the formation of II. It was found that in this case one ob-

*See [1] for Communication 23.

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